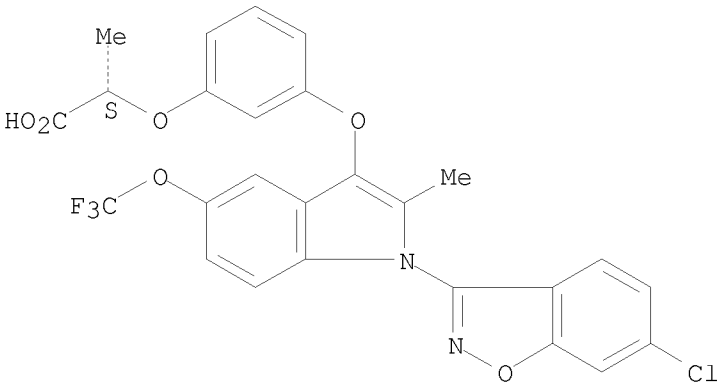
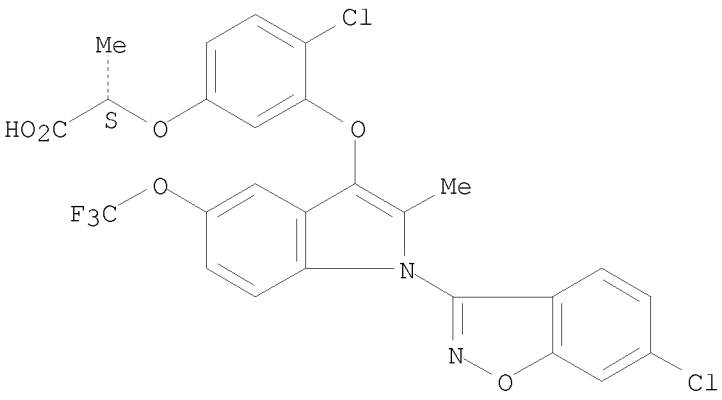
L11 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:378862 CAPLUS <<LOGINID::20080223>>
DN 143:78030
TI Selective PPARγ modulators with improved pharmacological profiles
AU Liu, Kun; Black, Regina M.; Acton, John J.; Mosley, Ralph; Debenham, Sheryl; Abola, Ramon; Yang, Meng; Tschirret-Guth, Richard; Colwell, Lawrence; Liu, Cherrie; Wu, Margaret; Wang, Chuanlin F.; MacNaul, Karen L.; McCann, Margaret E.; Moller, David E.; Berger, Joel P.; Meinke, Peter T.; Jones, A. Brian; Wood, Harold B.
CS Merck Research Laboratories, Rahway, NJ, 07065, USA
SO Bioorganic & Medicinal Chemistry Letters (2005), 15(10), 2437-2440
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 143:78030
AB A series of metabolically robust N-benzyl indole-selective PPARγ modulators with either a 3-benzoyl or 3-benzisoxazoyl moiety have been identified. In vitro, these compds. are partial agonists and exhibit reduced adipogenesis in human adipocytes. In vivo, these SPPARγMs (selective modulators) result in potent glucose lowering in db/db mice and attenuate increases in heart weight and brown adipose tissue that is typically observed in rats upon treatment with PPARγ full agonists.
IT 668489-67-6P 668489-97-2P 668490-04-8P
668490-08-2P 854933-09-8P 854933-10-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of (S)-[chloro[[(benzisoxazolyl)(trifluoromethoxy)indolyl]oxy]phenoxy]propanoic acid and study of its activity as partial agonist toward PPARγ)
RN 668489-67-6 CAPLUS
CN Propanoic acid, 2-[3-[[1-(6-chloro-1,2-benzisoxazol-3-yl)-2-methyl-5-(trifluoromethoxy)-1H-indol-3-yl]oxy]phenoxy]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



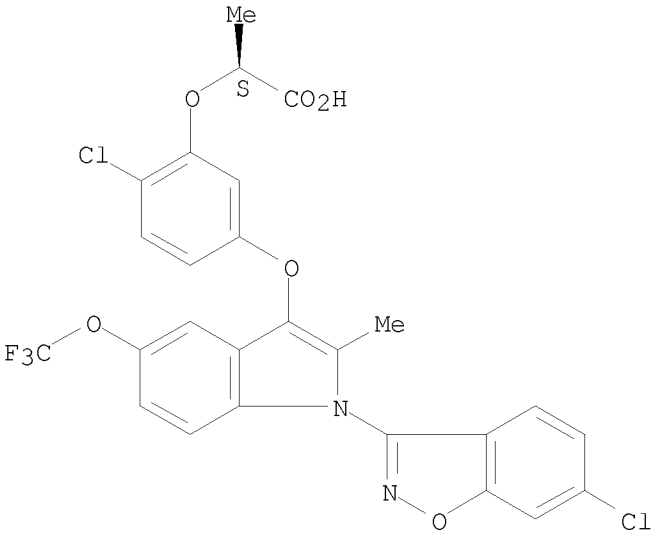
RN 668489-97-2 CAPLUS
CN Propanoic acid, 2-[4-chloro-3-[[1-(6-chloro-1,2-benzisoxazol-3-yl)-2-methyl-5-(trifluoromethoxy)-1H-indol-3-yl]oxy]phenoxy]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



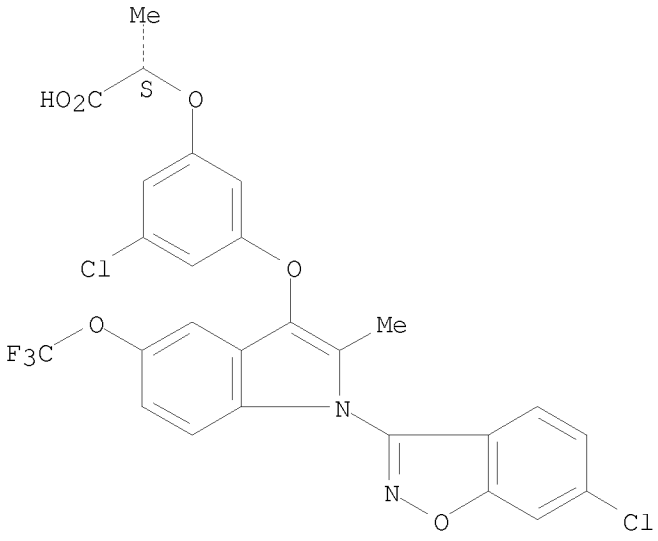
RN 668490-04-8 CAPLUS
CN Propanoic acid, 2-[2-chloro-5-[[1-(6-chloro-1,2-benzisoxazol-3-yl)-2-methyl-5-(trifluoromethoxy)-1H-indol-3-yl]oxy]phenoxy]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



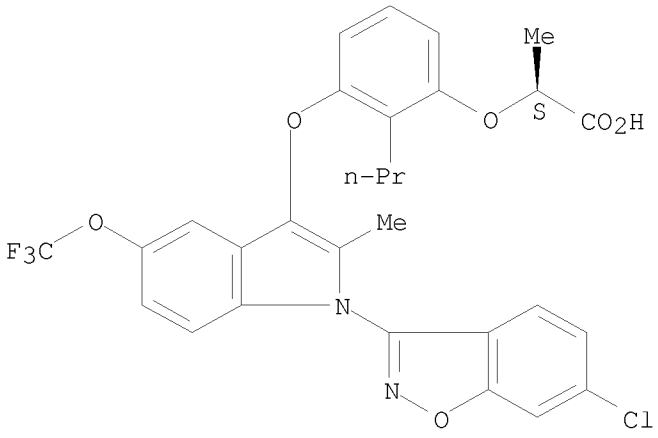
RN 668490-08-2 CAPLUS
CN Propanoic acid, 2-[3-chloro-5-[[1-(6-chloro-1,2-benzisoxazol-3-yl)-2-methyl-5-(trifluoromethoxy)-1H-indol-3-yl]oxy]phenoxy]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



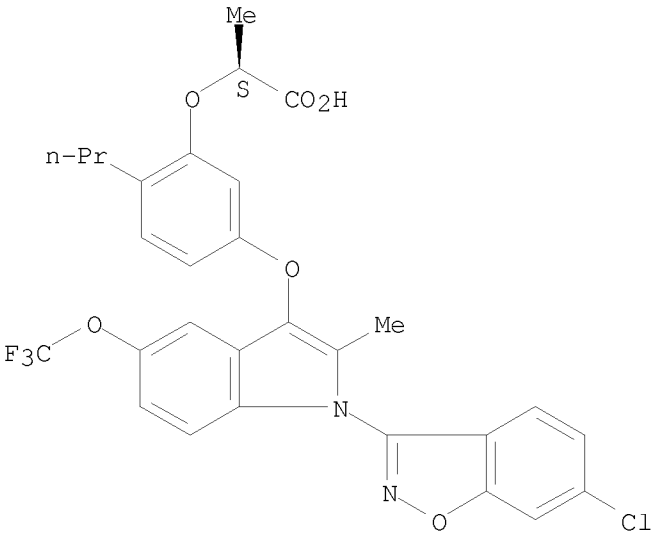
RN 854933-09-8 CAPLUS
CN Propanoic acid, 2-[3-[[1-(6-chloro-1,2-benzisoxazol-3-yl)-2-methyl-5-(trifluoromethoxy)-1H-indol-3-yl]oxy]-2-propylphenoxy]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 854933-10-1 CAPLUS
CN Propanoic acid, 2-[5-[[1-(6-chloro-1,2-benzisoxazol-3-yl)-2-methyl-5-(trifluoromethoxy)-1H-indol-3-yl]oxy]-2-propylphenoxy]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



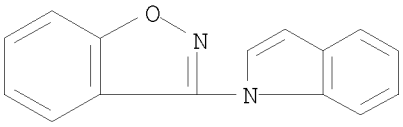
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:587625 CAPLUS <<LOGINID::20080223>>
DN 140:87002
TI Substituent effect on the reductive N-dearylation of 3-(indol-1-yl)-1,2-benzisoxazoles by rat liver microsomes
AU Tschirret-Guth, Richard A.; Wood, Harold B.
CS Department of Drug Metabolism & Basic Chemistry, Merck Research Laboratories, Rahway, NJ, USA
SO Drug Metabolism and Disposition (2003), 31(8), 999-1004
CODEN: DMDSAI; ISSN: 0090-9556
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB The reductive metabolism of a series of 3-(indol-1-yl)-1,2-benzisoxazoles was examined in vitro using rat liver microsomes. 3-(Indol-1-yl)-1,2-benzisoxazole was reduced to the corresponding amidine (resulting from N-O bond cleavage) under anaerobic conditions. The reaction required viable microsomes and NADPH and was inhibited by carbon monoxide, air, and ketoconazole, suggesting the involvement of cytochrome P 450 enzymes. The amidine was subsequently nonenzymically hydrolyzed to 1-salicylindole, which in turn was hydrolyzed to indole. Addition of electron-withdrawing substituents (Cl-, MeSO2-) at the 6-position of the benzisoxazole ring resulted in a significant increase in the rate of substrate reduction Introduction of electron-withdrawing substituents on the indole ring likewise increased the rate of substrate consumption but caused a substituent-dependent shift of the site of bond cleavage from the 1,2-isoxazole N-O bond to the C-N bond linking the 1,2-benzisoxazole to the indole moiety. In the case of 3-(2-chloro-3-methanesulfoxylindol-1-yl)-1,2-benzisoxazole, C-N bond cleavage was nearly quant., and products resulting from N-O bond reduction were not observed The overall rates of 3-(indol-1-yl)-1,2-benzisoxazoles reduction were found to be substrate concentration-dependent and observed Michaelis-Menten-type behavior. The apparent
Vmax of substrate reduction by rat liver microsomes correlated neg. with the free energy of the lowest unoccupied MOs (ELUMO) calculated semiempirically using a parameterized model 3 (PM3), and suggested that the initial

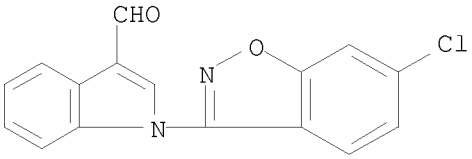
electron transfer was rate-determining and that the ELUMO could be used as an indication of the susceptibility of 1,2-isoxazoles to undergo reductive metabolism

IT 642477-86-9P 642477-89-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(substituent effect on the reductive N-dearylation of 3-(indol-1-yl)-1,2-benzisoxazoles by rat liver microsomes)

RN 642477-86-9 CAPLUS
CN 1,2-Benzisoxazole, 3-(1H-indol-1-yl)- (CA INDEX NAME)

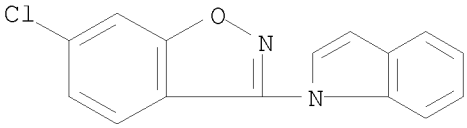


RN 642477-89-2 CAPLUS
CN 1H-Indole-3-carboxaldehyde, 1-(6-chloro-1,2-benzisoxazol-3-yl)- (CA INDEX NAME)

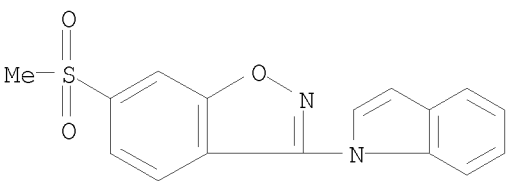


IT 642477-87-0P 642477-92-7P 642477-93-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(substituent effect on the reductive N-dearylation of 3-(indol-1-yl)-1,2-benzisoxazoles by rat liver microsomes)

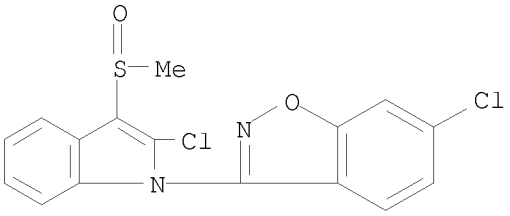
RN 642477-87-0 CAPLUS
CN 1,2-Benzisoxazole, 6-chloro-3-(1H-indol-1-yl)- (CA INDEX NAME)



RN 642477-92-7 CAPLUS
CN 1,2-Benzisoxazole, 3-(1H-indol-1-yl)-6-(methylsulfonyl)- (CA INDEX NAME)



RN 642477-93-8 CAPLUS
CN 1,2-Benzisoxazole, 6-chloro-3-[2-chloro-3-(methylsulfinyl)-1H-indol-1-yl]-
(CA INDEX NAME)



RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT